Implementation of EU Variations guidelines - EMA perspective

CASSS 2026

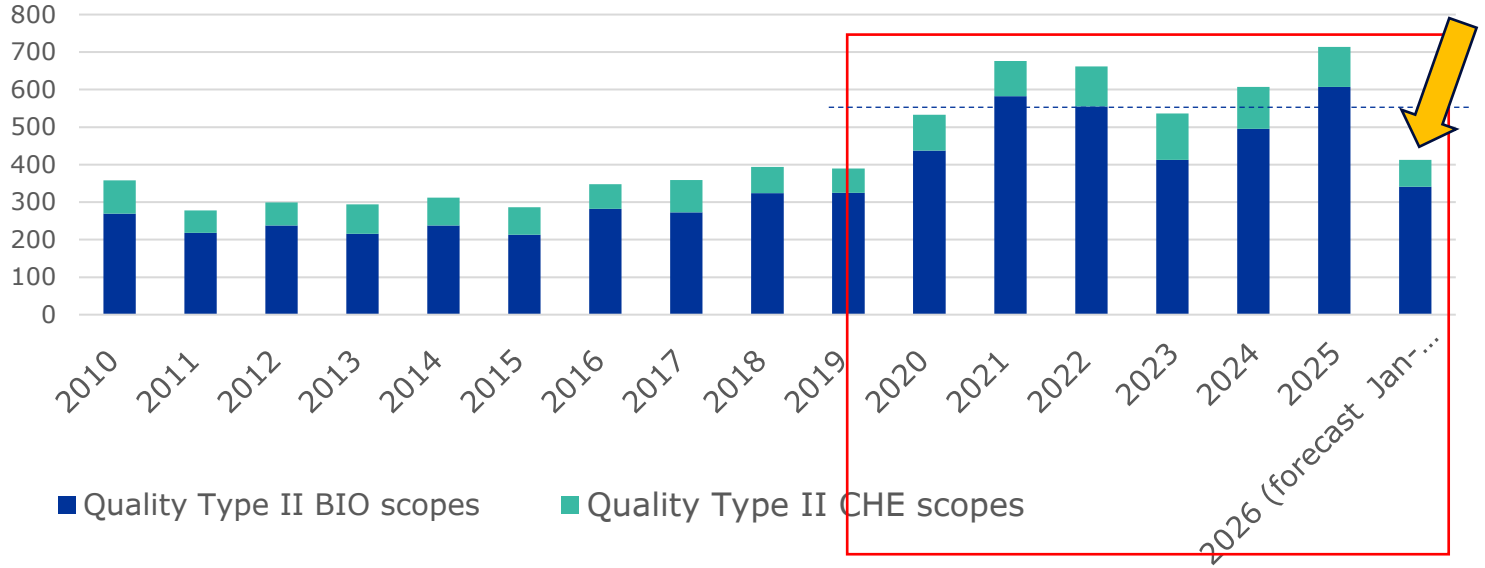
Prague, CZ

23 June 2026

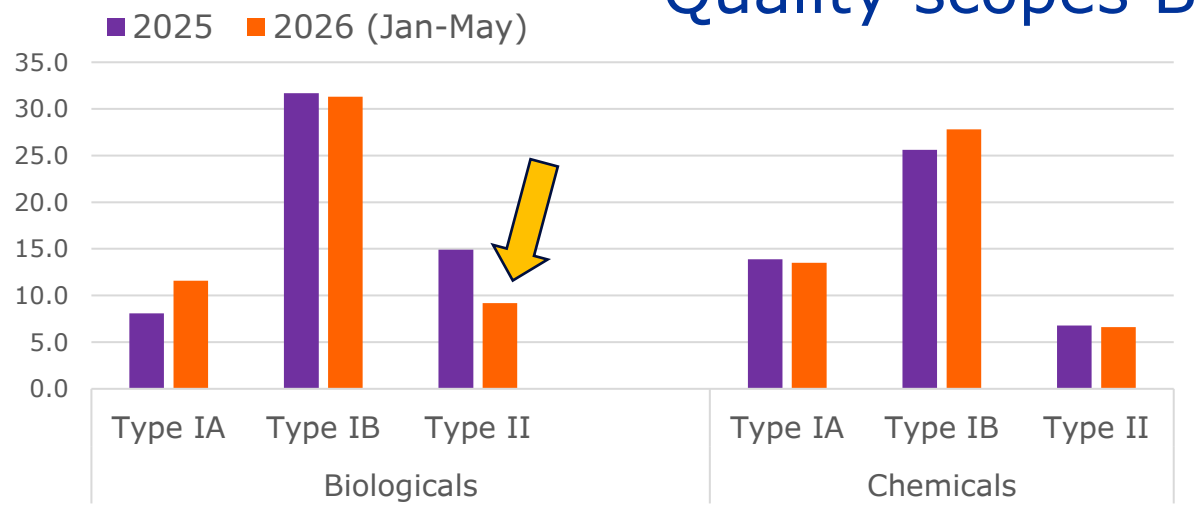
Elisa Pedone

Pharmaceutical Quality Office, EMA

Quality scopes over the years



Quality scopes BIO vs CHE



*scopes from Type IB and II procedures only

- ✓ Jan-May 2026: 36-32 % reduction in Quality type II submissions compared to 2020-2025 (mainly biologicals)
- ✓ Too early to draw firm conclusions
- ✓ Ongoing monitoring in 2026 to assess impact of new Variation classification GL
- ✓ Larger Groupings size observed
- ✓ Type II WS stable (already in use by MAH)
- ✓ Increase in IB WS (2025 vs 2024) driven by mandatory WS
- ✓ Within certain categories, increase in IBs due to downgrading of certain biosimilar scopes (e.g. QC sites)

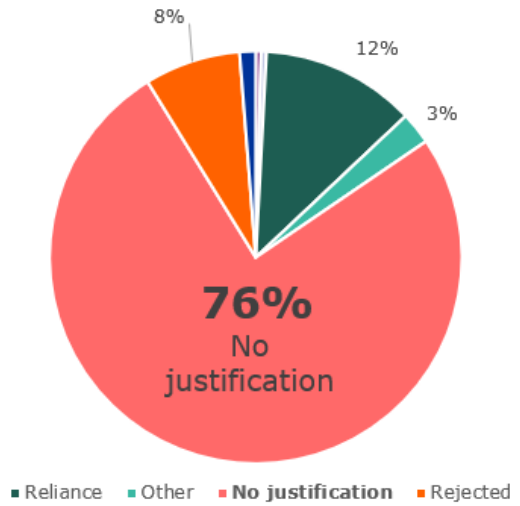
Experience with new Classification Guidance

- Most variations are correctly classified
- Some Type II variations can be downgraded
- Collecting experience on borderline IA outcomes (accepted/refused), especially where:
  - -BIO condition removed (e.g. minor manufacturing changes)
  - -Interpretations are not harmonised
- Extra decision steps for borderline cases increase workload, timelines, and uncertainty
- Complex IBs strain NCA expert allocation
- Large groupings add challenges and workload
- Ongoing EMA/NCA feedback collection to inform updates for next EC annual report

- ✓ No major classification issues identified
- ✓ Reinforce awareness of Q&As
- ✓ Continue monitoring classification trends
- ✓ NCAs are adapting to new Var Reg
- ✓ Avoid large groupings
- ✓ Develop new Q&As where clarity and harmonisation are needed
- ✓ EC to review findings and update Variations Guidelines accordingly

Conclusions on IA annual updates

- High share of IA procedures **outside the Annual update** during 2025 (46%), most (76%) without justification
- Grace period applied to facilitate transition
- Reminder: non-immediate Type IAs should be submitted as part of an annual update. **Justification** always required in exceptional individual submissions immediately after implementation (refer to Type-IA variations: Q&A)
- Overall IA decreasing, but not as expected
- Data not fully representative due to the implementation of the Variation classification guidelines on the 15th January 2026
- Strong compliance with the request to submit all IA ahead of the implementation of the new Variation classification



Practical recommendations on Annual Updates

- ✓ Provide a **clear** description of the **scope & classification** for all changes
- ✓ Include a clear "**present and proposed table**"
- ✓ Assess **cumulative impact** of grouped minor changes on criticality (not in isolation)
- ✓ **Extensive editorial updates** not suitable for annual update (IA notification) -> submit in IB/II procedures
- ✓ Use appropriate channels to ask questions Contacting EMA: post-authorisation | European Medicines Agency (EMA)

EMA/CMDh Q&As and guidelines to support implementation of revised variations guidelines

New & revised guidance:

- EMA/CMDh Guidance on the application of the revised variations framework (June 2025, Sep 2025)
- Update of CMDh guidance documents to reflect new Variation Guidelines (Oct 2025)
- Q&A on skip testing (Oct 2025)
- Q&A on novel or complex manufacturing process (Nov 2025)
- EMA's post-authorisation guidance e.g.:
  - Type IA/IB/II/Extension applications/grouping of variations (Nov 2025)
  - Classification of changes: Q&A (Nov 2025)
- Q&A regarding medicines used in combination with medical devices and consultation procedures by notified bodies (Nov 2025)
- Guidance on stability testing for applications for variations (December 2025)
- **Q&A on Post-Approval Change Management Protocol (PACMP) (December 2025)**
- **Q&A on Product Lifecycle Management document (PLCM) (January 2026)**
- Webinar on the new variations guidelines (13 January 2026)

Additional regulatory tools introduced under the revised variations framework

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Thank you

Follow us